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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/380,086	11/29/1999	PASCUAL PEREZ	BET-99/0730	2155

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YOUNG & THOMPSON
745 SOUTH 23RD STREET
2ND FLOOR
ARLINGTON, VA 22202

EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/380,086	PEREZ ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2004 and 17 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29,30 and 33-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29,30 and 33-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 27-34 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The rejection of claims 31-32 under 35 U.S.C. 103(a) as being unpatentable over Metz et al (1995, Mol. Breed. 1:309-317) in view of Vedel et al (1994, Plant Physiol. Biochem. 32:601-618) as applied to claims 27-28 above, and further in view of each of Welter (WO 98/06861) and Lenee et al (US 6,573,431, filed April 1996) is withdrawn in light of their cancellation.

4. The rejection of claims 29-30 and 33-34 under 35 U.S.C. 103(a) as being unpatentable over D'Halluin et al (US Patent 5,712,135, filed June, 1995) in view of Metz et al (1995, Mol. Breed. 1:309-317) and Welter (WO 98/06861). The rejection is modified from the rejection set forth in the Office action mailed 29 May 2003, as applied to claims 19 and 21-26. Applicant's arguments filed 1 December 2003 have been fully considered but they are not persuasive is withdrawn in light of Applicant's filing a translation of the priority document.

5. The rejection of claims 27-28 under 35 U.S.C. 103(a) as being unpatentable over Metz et al (1995, Mol. Breed. 1:309-317) in view of Vedel et al (1994, Plant Physiol. Biochem. 32:601-618) is withdrawn in light of their cancellation.

Claim Rejections - 35 USC § 112

6. Claims 29-30 and 33-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 24 February 2004, as applied to claims 27-34. Applicant's arguments filed 24 August 2004 have been fully considered but they are not persuasive.

Applicant urges that the specification teaches that any RNase may be appropriate, and that Vedel et al and EP 0 344 029 teach several RNases that can be used (response pg 6).

This is not found persuasive because the specification must describe male sterility genes within the full scope of the claims. The specification does not describe male sterility genes or RNAses within the full scope of the claims.

Applicant urges that the specification also teaches that RNases, endonucleases, proteases, cell wall inhibitors, ribozymes and other genes can be used (response pg 7).

This is not found persuasive because the specification must describe the structural features, not just the functional features, of these genes.

Applicant urges that the method is drawn to preventing a transgene integrated in a nuclear genome from being spread by pollen, and that dog gastric lipase and collagen are examples of such transgenes; however, Lenee teach other mammalian proteins that can be so expressed (response pg 7).

This is not found persuasive because the specification must describe the transgenes.

7. Claims 29-30 and 33-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for preventing dissemination of a transgene encoding dog gastric lipase wherein the transgene is on the same vector as the barnase or glucanase male sterility genes, does not reasonably provide enablement for methods for

preventing dissemination of any transgene of interest wherein the methods use any artificial male sterility gene expressed from any promoter, and/or a transgene encoding any therapeutic or prophylactic compound of human or animal origin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the Office action mailed 24 February 2004, as applied to claims 27-34. Applicant's arguments filed 24 August 2004 have been fully considered but they are not persuasive.

The claims are broadly drawn to methods for preventing dissemination of any transgene of interest wherein the methods use a maize, rape or tomato plant with cytoplasmic male sterility, any artificial male sterility gene, and/or a transgene encoding any therapeutic or prophylactic compound of human or animal origin.

The instant specification, however, only provides guidance for construction of plant transformation vectors comprising a gene conferring male sterility, comprising the A9 promoter operably linked to either the glucanase or the barnase gene, a gene encoding dog gastric lipase, and a gene conferring resistance to Basta (examples 1-2); and transformation of the vectors into *Brassica napus* (example 3) and tobacco (example 4). The instant specification also provides guidance for construction of a plant transformation vectors comprising the Ac transposase gene (example 5) and one presumably comprising the A9 promoter operably linked to the glucanase gene and excision sequences (example 6); transformation of the vector of examples 5 and 6 into separate tomato plants (example 7); constructing a vector comprising a Ds element inserted into the Gus gene, transforming this into plants and showing that the plants produced blue spots, *i.e.*,

that the Ds element was excised (example 8); and generation of T2 seeds that contain an unidentified transgene (example 9). The instant specification also provides guidance for crossing male sterile plants containing the Ds element and an unknown artificial male sterility gene to plants expressing the Ac transposase (example 10); identification of the excision event in F1 plants by PCR to determine which no longer have the AMS gene - such plants in an unexplained manner also lack the transposase gene but have an undefined gene of interest (example 11); and construction of a plant transformation vectors containing the FLP recombinase (example 12) and the one containing a A9-barnase male sterility gene and a kanamycin resistance gene between FRT recombination sites (example 13).

It is noted that following what exactly was done in the examples and what each vector and plant comprises is very difficult, and in some cases impossible, to determine from the specification.

The instant specification fails to provide guidance for artificial male sterility genes other than the glucanase or the barnase gene, transgenes encoding a therapeutic or prophylactic compound of human or animal origin other than dog gastric lipase, or any maize, rape or tomato plant with cytoplasmic male sterility.

Additionally, the claims are drawn to expression of the male sterility gene from any promoter. A promoter that targets expression of the gene to male plant parts must be used.

Given the claim breath and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate methods for preventing dissemination of any transgene of interest wherein the methods use a maize, rape or

tomato plant with cytoplasmic male sterility, any artificial male sterility gene, and/or a transgene encoding any therapeutic or prophylactic compound of human or animal origin.

Applicant urges that the specification teaches that any RNase may be appropriate, and that Vedel et al and EP 0 344 029 teach several RNases that can be used (response pg 6).

This is not found persuasive because the specification must teach male sterility genes within the full scope of the claims. The specification does not teach male sterility genes or RNAses within the full scope of the claims.

Applicant urges that the specification also teaches that RNases, endonucleases, proteases, cell wall inhibitors, ribozymes and other genes can be used (response pg 7).

This is not found persuasive because the specification must teach these genes.

See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Applicant urges that the method is drawn to preventing a transgene integrated in a nuclear genome from being spread by pollen, and that dog gastric lipase and collagen are examples of such transgenes; however, Lenee teach other mammalian proteins that can be so expressed (response pg 7).

This is not found persuasive because it is the specification that must teach these genes.

8. Claims 29-30 and 33-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that

Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is repeated for the reasons of record as set forth in the Office action mailed 24 February 2004, as applied to claims 27-34. Applicant's arguments filed 24 August 2004 have been fully considered but they are not persuasive.

Claims 29 and 30 are indefinite in their recitation of "artificial male sterility (AMS) gene" in lines 6-7. It is unclear what it means for a male sterility gene to be artificial - in what manner is it artificial? It is also unclear how artificial male sterility genes differ from naturally occurring ones, and if naturally occurring ones are excluded.

Applicant urges that "artificial" does not characterize the gene per se, but male sterility, and male sterility results from human transformation of the plant, and notes that WO 96/26283 also uses this term (response pg 8-9).

This is not found persuasive. If this is what applicant intends, it is suggested that "artificial male sterility gene" or its equivalent in the claims, be replaced with --a gene conferring male sterility--

Claims 28-29 are indefinite in their recitation of "therapeutic or prophylactic compound". Some compounds are therapeutic or prophylactic in some circumstances and toxic or ineffective in others. It is unclear if those compounds are included.

Applicant urges that the term is definite to one of skill in the art and that the invention is a method of preventing the spread of a transgene in a plant cultivated for production of compounds of therapeutic or prophylactic interest, that is compounds that are intended for use in humans or animals; that a compound may be toxic in some circumstances does not preclude it being therapeutic or prophylactic under others (response pg 9).

This is not found persuasive because the specification does not define therapeutic or prophylactic compounds as compounds that are intended for use in humans or animals

Claim Rejections - 35 USC § 103

9. Claims 29-30 and 33-36 rejected under 35 U.S.C. 103(a) as being unpatentable over D'Halluin et al (US Patent 5,712,135, filed June, 1995) in view of Metz et al (1995, Mol. Breed. 1:309-317) and Lenee et al (US 6,573,431, filed April 1996).

The claims are drawn to methods of transforming plants with constructs comprising an AMS gene and a gastric lipase gene, with the goal of preventing spread of the gastric lipase gene by pollen.

D'Halluin et al disclose transformation of maize with the barnase gene linked to a transgene of interest, the kanamycin resistance gene or the bar gene (column 19, line 47, to column 23, line 36). D'Halluin et al do not disclose transformation with a gene encoding gastric lipase.

Metz et al teach that the advantage of transforming male-sterile lines is that there is no danger of gene transfer to other plants through pollen (pg 315, right column, paragraph 3).

Lenee et al teach transformation of plants, including corn and rape, with a gene encoding dog gastric lipase (claim 10). The gastric lipase would be administered to a human or animal (abstract; column 3, lines 60-63).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of transformation as taught by D'Halluin et al to transform the plants with a gene encoding gastric lipase, as taught by Welter. One of ordinary skill in the art

would have been motivated to do so because of the teachings of Metz et al that the advantage of transforming male-sterile lines is that there is no danger of gene transfer to other plants through pollen (pg 315, right column, paragraph 3) and the suggestion of D'Halluin et al to transform the plants with economically important proteins (column 10, lines 43-46).

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Anne R. Kubelik, Ph.D.
November 18, 2004

ANNE KUBELIK
PATENT EXAMINER